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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 12/12/2002 17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/924,396	KIRSCH ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *1-7,11 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-10 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3, 14, 1* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group XVI in Paper No. 16 is acknowledged. The traversal is on the ground(s) that Groups XVI and XVII both comprise the same claims and are directed to detection of IRP protein "regardless of whether the method detects the protein itself or the nucleic acid that encodes for the protein". This is not found persuasive because an application may properly be required to be restricted to one of two or more claimed inventions if they are able to support separate patents and they are either independent (MPEP § 806.04 - § 806.04 (j)) or distinct (MPEP § 806.05 - § 806.05 (i)). The Examiner has shown that the Groups XVI and XVII are independent or distinct for the reasons in the previous Office action (see Paper No. 13). Furthermore, MPEP § 803 provides that the separate classification (i.e., class and subclass) of distinct inventions is sufficient to establish a *prima facie* case that the search and examination of the plural inventions would impose a serious burden upon the Examiner; such separate classification was set forth in the Office action mailed July 18, 2002 (Paper No. 13).

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-6, 11-17 and 19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 16.

Claims 7-10 and 18, in so far as they are directed to a method of identifying a subject in need of treatment of a neurodegenerative disease by using a probe that interacts with IRP-2 protein, are under examination in the instant office action.

Specification

2. The text of the instant specification is not in compliance with the requirements for Sequence Identifiers (see MPEP 2422.03). The appropriate format for sequence identifiers is SEQ ID NO:X, wherein "X" is the sequence number. Appropriate correction is required.

3. The use of the trademarks has been noted in this application, see page 30, line 1, page 38, line 14 and page 49, line 6, for example. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicant is advised to review the entire text of the instant specification for other possible use of trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 7-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 7-10 are directed to a method of identifying a subject in need of treatment or prevention of a neurodegenerative disease by determining the presence or absence of interaction of a probe with a wild type or mutant IRP-2 protein. It is known from the prior art that iron regulatory proteins (IRP) are "cytoplasmic mRNA binding proteins that respond to cellular iron concentrations by regulating the translation of proteins involved in iron uptake" (see Smith et al., Brain Research, 1998, 788, pp.232-236; reference provided in IDS of Paper No. 3, specifically at page 232, part Introduction). The instant specification fails to provide any guidance on how to detect wild or mutant IRP-2 protein in any biological sample, the examples of which can include saliva or urine samples.

Further, one of ordinary skill in the art readily recognizes that an antibody, or a probe, that binds to IRP-2 protein would most probably identify IRP-2 in a biological sample, such as a sample of nervous tissue, of any control subject, because there is no known reports of IRP-2 being specifically or exclusively associated with neurodegenerative diseases. On the contrary, the art teaches that "[c]ontrol brains show little IRP-2 immunoreactivity, confirming previous studies of normal brain" (Smith et al., p.234, Discussion). The instant specification fails to provide any evidence or sound scientific reasoning that would support a conclusion that detection of IRP-2 protein is associated with any neurodegenerative disease; therefore, one of ordinary skill in the art would have no basis for concluding that "determining the presence" of the probe" (claim 7) would lead to identification of a subject in need of treatment of a neurodegenerative disease.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of

direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. In re Wands, 8 USPQ2d, 1400 (CAFC 1988).

The instant invention is based on "the discovery that mutations in the IRP-2 gene result in forms of IRP-s proteins that resist degradation in the body and, thereby, perturb iron homeostasis" (page 6, lines 20-21 of the instant specification). Claims 7-10 are drawn to a method of identifying a subject in need of treatment or prevention of a neurodegenerative disease. However, the term "neurodegenerative disease" is very broad and includes diseases of different etiology, such as neurodegeneration resulting from acute trauma or infectious disease. One skilled in the art readily recognizes that neurodegenerative diseases that originated from trauma or infection most probably would not be associated with abnormal iron-dependent oxidation within a peptide loop of IRP-2 protein.

Further, although the prior art describes that interruption in brain iron regulation can be associated with some neurodegenerative diseases, Alzheimer's disease in particular, no indication can be found in prior art that would lead to a conclusion that mutations in IRP-2 gene specifically are associated with neurodegenerative diseases in general or would define predisposition to development of a neurodegenerative disease. Thus, the art is unpredictable on the subject of correlation of mutations in IRP-2 gene and neurodegeneration in general. The instant specification fails to present any sound scientific reasoning or any evidence that such correlation indeed exists for any of the neurodegenerative diseases. There are no working examples to support the claimed method, except for a proposed general scheme of future analysis

of peripheral blood samples from MCI (mild cognitive impairment syndrome) patients (page 62-64, Example 6 of the instant specification).

The standard of an enabling disclosure is not the ability to make and test if the invention worked but one of the ability to use with a reasonable expectation of success. The instant specification as originally filed provides no guidance and no working examples on how to practice the claimed invention. Thus, in view of the lack of teachings and unpredictability of the art set forth earlier, the instant specification is not found to be enabling for a method of identifying a subject in need of treatment or prevention of a neurodegenerative disease. It would require undue experimentation and making a substantial inventive contribution for the skilled artisan to discover how to use Applicants' invention as currently claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 7-10 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 7 is vague and indefinite for recitation of IRP-2. It is suggested that the full name of IRP-2 is used followed by the abbreviated name. Furthermore, the claim is indefinite in so far as it employs the term "IRP-2" as a limitation. It appears that IRP-2 can be represented by different molecular embodiments, therefore, without a reference to a precise amino acid sequence identified by a proper "SEQ ID NO:" one cannot determine the metes and bounds of "IRP-2". Moreover, because the instant specification does not identify the property or

combination of properties which are unique to and, therefore, definitive of a "IRP-2", an artisan cannot determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation.

Claim 7 is also indefinite for recitation "a biological sample from [a]subject having polynucleotides or protein". It is confusing if a sample or a subject is having polynucleotides or protein. Clarification is required.

Claim 7 is further vague and ambiguous because it is not clear what is the determining step for identification of a subject in need of treatment or prevention of a neurodegenerative disease. Is it "detecting the amount of probe that interacts with the protein" or is it the determination of the presence or absence of the probe"? Clarification is required.

Lastly, claim 7 is indefinite because recitation "determining the presence or absence of the probe with the polynucleotide or protein in the biological sample" does not make sense. Clarification is required.

7. Claim 18 is vague and ambiguous because the claim does not make sense. It is suggested that the claim is rewritten so that the metes and bounds of the claimed subject matter can be determined from the claim.

8. Claims 8-10 are indefinite for being dependent from indefinite claim.

Conclusion

9. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D.
December 10, 2002

JOHN ULM
PRIMARY EXAMINER
GROUP 1800